REMARKS

Claims 1, 4-7, 11, 21-27, and 30-44 are pending in the application. Claims 2, 3, 8-10, 12-20, 28, and 29 have been canceled without prejudice, and claims 5, 7, 22, 25, 38, and 42 have been amended. Support for the amendments can be found in the specification at, e.g., page 47, lines 6-25. These amendments add no new matter.

Priority Claim

At page 2 of the Office Action, the Examiner alleged that priority provisional application number 60/318,645, filed September 10, 2001 (the '645 application), "does not provide support for nucleic acids encoding a nucleotide sequence which is 85%, 95% or 98% identical to SEQ ID NO:6 or nucleic acid sequences which hybridize under conditions of instant claim 5 to SEQ ID NO:5." On this basis, the Examiner asserted that claims 5, 22-29, 35, and 37-40 are not entitled to the priority date of the '645 application.

Contrary to the Examiner's assertions, the '645 application provides support for all claims pending in the present application. In particular, support for the percent identity and hybridization language of claims 5, 22-29, 35, and 37-40 can be found in the '645 application at, e.g., page 8, lines 5-9; page 11, lines 5-9; page 22, lines 17-27; and page 44, lines 1-6.

In light of these comments, applicants request that the Examiner acknowledge that the '645 application provides support for all claims of the present application.

Objections to the Specification

At page 2 of the Office Action, the Examiner objected to the specification as containing blank spaces after occurrences of "ATCC." The blank spaces were inserted in the application to allow for the later introduction of deposit information. Upon notification that the claims are in condition for allowance, applicants will amend the specification to either insert deposit information or remove the blank spaces.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 2-6 of the Office Action, the Examiner rejected claims 5, 22-33, and 35-44 as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that applicant had possession of the claimed invention at the time of filing.

(i) Hybridization

In rejecting claims 5, 28, and 29, the Examiner stated that the claims are

> drawn to a genus of isolated nucleic acids which hybridizes to SEQ ID NO:5 under conditions of incubation at 45 degrees in 6.0X SSC followed by washing in 0.2X SSC/0.1% SDS at 65 degrees. The genus of nucleic acids are not limited by the functional attributes of what is encoded by the hybridizing nucleic acid. Thus, the genus is variant, encompassing nucleic acids which encode mutant, truncated and allelic variants of SEQ ID NO:5. The specification set for SEQ ID NO:5 as encoding SEQ ID NO:6. With the exception of degenerate coding sequences of SEQ ID NO:5, the specification does not provide adequate written description for the genus of nucleic acids which would hybridize under the recited conditions to SEQ ID NO:5 because the genus includes nucleic acids which encode proteins having widely different functional attributes for the instant SEQ ID NO:6.

Claims 28 and 29 have been canceled, thereby rendering their rejection moot.

Amended claim 5 is drawn to a nucleic acid containing a nucleotide sequence that:
(a) hybridizes to SEQ ID NO:5 or the complete complement thereof under conditions of incubation at 45°C in 6.0X SSC followed by washing in 0.2X SSC/0.1% SDS at 65°C; and
(b) encodes a polypeptide that stimulates apoptosis.

The genus of nucleic acids encompassed by claim 5 does not have substantial variation, since each nucleic acid must encode a polypeptide that has a specified activity (i.e., the ability to stimulates apoptosis) and contain a structurally similar nucleotide sequence (i.e., one that hybridizes under the hybridization and washing conditions recited in the claims). The PYRIN-5 nucleic acid of SEQ ID NO:5 disclosed in the specification is representative of the claimed genus because: all members of the genus hybridize under high stringency to a PYRIN-5 nucleic acid; and the skilled artisan can readily perform assays for identifying variants encompassed by the

claim having the specified activity. In light of this disclosure, the skilled artisan would have concluded, at the filing of the present application, that applicant was in possession of the necessary common attributes possessed by the members of the genus.

The Examiner cited *Regents of the University of California v. Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) in support of the present rejection. The discussion in *Lilly* regarding a proper written description for genus claims had to do with a claim drawn to a vertebrate mRNA encoding insulin. The *Lilly* court held that a generic statement, such as the term "mammalian insulin cDNA" is not, without more, an adequate written description of an invention claiming the nucleotide sequence for human insulin. The court's decision in *Lilly* focused on functional claims directed merely to a desired result without structure: "[t]he description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention." *Id.* at 1406. However, the *Lilly* court also took care to indicate that structural information about the claimed genus was different in kind than a mere desired result. The court indicated that in claims involving chemical materials such as proteins and polynucleotides "generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is usually an adequate description of the claimed genus." *Id.*

The present claims are drawn to nucleic acids identified, in part, by their ability to hybridize to a reference polynucleotide sequence under a set of defined hybridization and washing conditions. The ability of a nucleic acid molecule to hybridize to a reference nucleic acid molecule under such defined conditions is dependent on the structure (sequence) of the nucleic acid molecule. Moreover, the claimed nucleic acids are also defined by the recited function of the polypeptide encoded by the nucleotide sequence (i.e., the ability to stimulate apoptosis). The claims are not directed to a desired result without structure, as was the case in *Lilly*. A person of ordinary skill in the art would clearly understand the structural definition of the nucleic acids provided by the claims and would therefore understand applicant to have been in possession of the claimed nucleic acids at the time the application was filed. Accordingly,

applicants respectfully submit that the pending "hybridization" claims satisfy the written description requirement.

(ii) Nucleic Acid Encoding a Polypeptide Containing a Specific Functional Domain of PYRIN-5

In rejecting claims 30-33, the Examiner stated that

> [t]he claims are drawn to a genus of nucleic acids which encode proteins which minimally comprise a pyrin, NBS or LRR domain of SEQ ID NO:6. The genus of nucleic acids encompassed by the claims is highly variant because numerous structural alterations are tolerated in the proteins encoded by the nucleic acids and the genus tolerated members which encode proteins having numerous functional attributes which differ from those of SEQ ID NO:6. The disclosure of polynucleotide encoding SEQ ID NO:6 does not adequately describe the claimed genus which includes nucleic acids encoding protein which differ both structurally and functionally from the instant SEQ ID NO:6.

The present application describes the identification and characterization of PYRIN-5. PYRIN-5 has an N-terminal pyrin domain (at about amino acid residues 1-91 of SEQ ID NO:6), a central nucleotide binding site ("NBS") domain (at about amino acid residues 188-506 of SEQ ID NO:6), and a C-terminal leucine rich repeat ("LRR") domain (at about amino acid residues 688-1056 of SEQ ID NO:6) (see Table 4 at page 36 of the specification). PYRIN-5 belongs to the NACHT (NAIP, CIIA, HET-E and TP1) subfamily of NBS-domain containing proteins (see, e.g., specification at page 5, lines 1-9 and Koonin et al. (2000) Trends Biochem. Sci. 25:223). Members of the NACHT NTPase subfamily have been implicated in apoptosis.

Claims 30-33 are directed to nucleic acids containing a nucleotide sequence that encodes a polypeptide containing amino acid residues 1-91 (pyrin domain), 188-506 (NBS domain), or 688-1056 (LRR domain) of the PYRIN-5 sequence of SEQ ID NO:6.

The precise structural definition of the polypeptides (comprising amino acid residues that correspond to the pyrin domain, NBS domain, or LRR domain of PYRIN-5) encoded by the nucleic acids of claims 30-33 allows the skilled artisan to readily envision the claimed invention and understand that applicant invented what is claimed. The polypeptides encoded by the nucleic acids of claims 30-33 are described in the specification at, for example, page 13, line 12,

to page 14, line 9. Because the polypeptides encoded by the claimed nucleic acids contain a particular functional domain of PYRIN-5, the polypeptides necessarily retain the functional activity present in the recited portion of PYRIN-5. Polypeptides containing such functional regions of PYRIN-5 can be used, for example, in screening for compounds that modulate a PYRIN-5 activity associated with that particular region. For example, a polypeptide containing amino acids 188-506 of SEQ ID NO:6 (NBS domain) of PYRIN-5 necessarily has nucleotide-binding activity, and can therefore be used to screen for compounds that modulate the ability of PYRIN-5 to bind to a nucleotide.

In light of the above, applicants submit that the polypeptides encoded by the nucleic acids of claims 30-33 are amply described in the specification, both in terms of structure and associated function, such that the skilled artisan would readily understand applicants to have been in possession of the claimed invention at the time of filing of the present application. Accordingly, applicants request that the Examiner withdraw the rejection.

(iii) Percent Identity

Amended claims 22-24 are drawn to a nucleic acid containing a nucleotide sequence that encodes a polypeptide that: (a) stimulates apoptosis; and (b) contains an amino acid sequence that is at least 85% identical to the sequence of SEQ ID NO:6. In addition, amended claims 25-27 are drawn to a nucleic acid containing a nucleotide sequence that: (a) encodes a polypeptide that stimulates apoptosis; and (b) is at least 85% identical to the sequence of SEQ ID NO:5.

The PYRIN-5 nucleic acids disclosed in the specification are representative of the claimed genus because: all members of the genus contain or encode a sequence highly similar to a reference sequence (SEQ ID NO:5 or SEQ ID NO:6); and the skilled artisan can readily carry out assays for identifying variants encompassed by the claim that have the ability to stimulate apoptosis. In light of this disclosure, the skilled artisan would have concluded, at the filing of the present application, that applicants were in possession of the necessary common attributes possessed by the members of the genus.

Similar to the discussion above with respect to the "hybridization" claims, the specification provides relevant identifying characteristics of the claimed nucleic acid molecules. The present claims are drawn to nucleic acids structurally defined by their degree of identity to a reference sequence. The claims thus provide a precise definition of the invention by structure. Moreover, the claimed nucleic acids are also defined by the recited function of the polypeptide encoded by the nucleotide sequence (i.e., the ability to stimulate apoptosis). The claims are not directed to a desired result without structure, as was the case in *Lilly*. A person of ordinary skill in the art would clearly understand the structural definition of the nucleic acids provided by the claims and would therefore understand applicant to have been in possession of the claimed nucleic acids at the time the application was filed. Accordingly, applicants submit that the pending "percent identity" claims satisfy the written description requirement.

35 U.S.C. §112, First Paragraph (Enablement)

At pages 6-8 of the Office Action, the Examiner rejected claims 7, 38, 39, 42, and 43 as allegedly not enabled. The Examiner stated that amending the claims to recite and "isolated" cell would overcome the rejection.

Claims 7, 38, and 42 have been amended to recite an "isolated host cell." Claims 39 and 43 depend from claims 38 and 42, respectively. In light of these amendments, applicants request that the Examiner withdraw the rejection.

35 U.S.C. §102(e) (Anticipation)

At pages 8-9 of the Office Action, the Examiner rejected claims 5, 28-33, and 36 as allegedly anticipated by Ramkumar et al., WO 02/48362 ("Ramkumar"). According to the Examiner,

> Ramkumar et al disclose Sequence identifier 3 consisting of at least 1000 nucleotides which would hybridize to the instant SEQ ID NO:5. Said Sequence Identifier 3 encodes a polypeptide which comprise residues 1-91, 188-506 and 688-1056 of SEQ ID NO:6.

As detailed in the "Priority Claim" section above, all claims pending in the present application are entitled to the September 10, 2001 priority date of the '645 priority application.

Ramkumar was filed on November 14, 2001 and claims priority to U.S. provisional application number 60/249,407, filed November 15, 2000. The Examiner listed U.S. provisional application number 60/249,401 in the Non-Patent Documents section of form PTO-892 and enclosed a copy of application number 60/249,401 with the Office Action. However, application number 60/249,401 is not a priority document for Ramkumar and has no apparent connection to the cited PCT application (application number 60/249,401 is entitled "Retractable Rod Screens"). The underlined portions of the preceding application numbers indicate the differences between serial numbers of the Ramkumar priority application and the provisional application cited in the present Office Action.

Because Ramkumar was filed (November 14, 2001) after the priority date of the pending claims (September 10, 2001), any material present only in the Ramkumar PCT filing (and not in the priority provisional application) does not constitute 102(e) art against the present application. If the Examiner wishes to maintain the present rejection, applicants respectfully request that the Examiner supply (a) a copy of application number 60/249,407; and (b) any alignments used in comparing sequences of the present application with those of application number 60/249,407.

Because applicants were not supplied a copy of the priority application of Ramkumar, and are thus unable to comment on the relevance of that application to the present rejection, any subsequent action that corrects this defect and supplies a copy of application number 60/249,407 should be a non-final Office Action (since such an action would be necessitated by the Examiner's mistake in sending the wrong priority application).

CONCLUSION

Applicants ask that all claims be allowed in view of the amendments to the claims and the remarks contained herein.

Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 16953-002001.

Respectfully submitted,

Date: November 1, 2004

Jack Brennan
Reg. No. 47,443

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (212) 258-2291